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Formation mechanisms of disinfection byproducts: Recent developments

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Abstract

Water disinfection is used in drinking water treatment to protect public health by controlling microbial pathogens that cause waterborne diseases. Water disinfectants also react with natural organic matter found in source waters to unintentionally produce disinfection byproducts (DBPs). However, with increasing populations and climate change, water sources are receiving anthropogenic inputs that differ from natural organic matter. These changes trigger the formation of a new suite of DBPs with unknown formation mechanisms. This review provides an overview of recent research on DBP formation mechanisms and analytical methods of priority DBPs including *N*-halamines, organic and inorganic amines, nitrosamines, total organic halogen, and DBPs derived from advanced oxidation processes including combined UV/chlorine processes. Key intermediates responsible for DBP formation which were previously unnoticed and new analytical method developments are also highlighted.

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Disinfection byproducts, Formation mechanisms, N-DBPs, UV/chlorine, *N*-halamines.

Introduction

For more than a century, chemical disinfectants have been used in water treatment to effectively control pathogens, thereby reducing waterborne diseases worldwide [1]. However, disinfectants also react with natural organic matter and inorganic ions (i.e. bromide and iodide) present in source waters to unintentionally form disinfection byproducts (DBPs). Long-term exposure to DBPs has been shown to pose health problems including bladder cancer and adverse birth defects [2–4]. Although more than 600 DBPs have been identified in literature [5], DBP formation mechanisms still remain largely uncharacterized. Furthermore, with an increasing population and changing climate dynamics, water quality sources will continue to evolve, and as a consequence, DBP precursors will also vary. These changes may create an entirely different suite of DBPs with unknown formation mechanisms.

Significant computational and experimental efforts are needed to characterize DBP formation mechanisms. These efforts may include identification of DBP precursors, quantification of DBPs and intermediates, characterization of chemical formation pathways, determination of kinetic rate constants and/or reaction activation energies, and development of kinetic or computational models that can predict DBP formation under varying water quality conditions [6]. Given the extent of these efforts, priority is typically given to DBPs with high toxicities or, alternatively, those with unknown toxicities relevant to human health but with widespread occurrence in drinking water. A few recent articles provide a current analysis of DBP research and human health on the basis of existing knowledge and future needs [7–9]**. Priority DBPs include nitrogen-containing DBPs (N-DBPs), iodinated-DBPs, and DBPs derived from new advanced oxidation processes (AOPs) such as combined UV/chlorine and UV/chloramine. This review highlights top research on formation mechanisms for these priority DBPs published between January 2016 and March 2018, excluding iodinated DBPs which have been recently discussed in detail by Postigo and Zonja [10].

Nitrogen-based DBPs

Organic *N*-halamines

Organic *N*-halamines are halogenated organic compounds that are formed by the reaction of dissolved organic matter (DOM) with oxidants (i.e. chlorine, combined chlorine, bromine, or iodine). The nitrogen inorganic *N*-halamines can originate from DOM or the oxidant. How et al. [11]* published a critical review on the formation, stability, toxicity, and analysis of *N*-chloramines. The formation and degradation pathways for *N*-chloramino acids, *N*-chloraldimines, *N*-

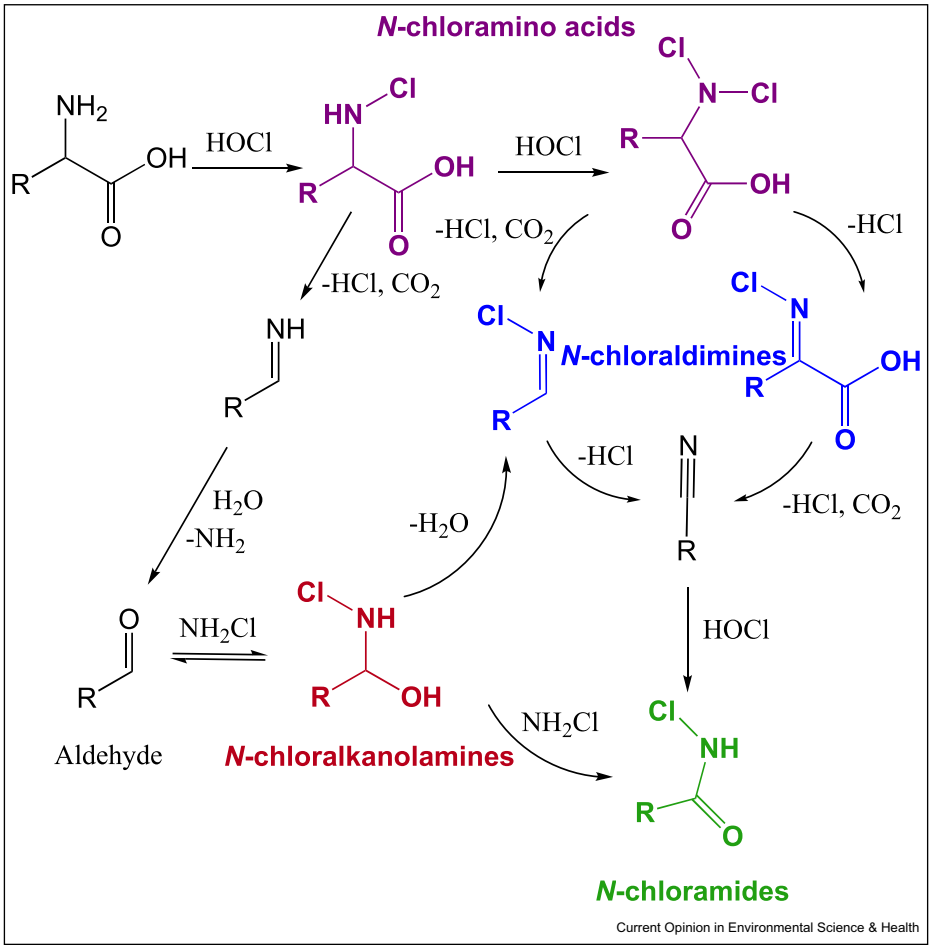
chloralkanolamines, and *N*-chloramides are summarized in Figure 1. The authors identified a knowledge gap including the unknown formation of organic *N,N*-dichloramines. The same research group conducted a detailed investigation on the mechanism of the reaction between chlorine and the amino acid valine [12]. *N*-monochlorovaline and *N,N*-dichlorovaline were identified as two major intermediates which further degraded into an aldehyde, a nitrile, and *N*-chloraldimines (Figure 1). *N*-chloraldimines are of particular concern because they have the potential to form at higher levels than their odor threshold concentrations.

Another significant challenge in the study of *N*-chloramines is the lack of appropriate analytical methods that arises due to their high instability and reactivity. For example, *N*-chloramides are quickly destroyed on reaction with quenchers used in water analysis, thereby rendering them undetectable. However, recent efforts have focused on the development of new analytical methods for organic *N*-chloramines [13,14]. Recent advances in method development aim to overcome the detectability of the unstable N—Cl bond in *N*-chlorinated dipeptides using liquid chromatography high-resolution mass spectrometry [13]. To differentiate the N—Cl bond in *N*-chlorinated dipeptides from their C—Cl analogous, water samples were analyzed before and after treatment with ascorbic acid [14]. The difference in these analyses correlates with the N—Cl fragment of *N*-chlorinated dipeptides, thereby establishing new methods to identify *N*-halamines in water samples. Additionally, two chemical *N*-halamide formation pathways were identified from the reaction of aldehydes and monochloramine [15,16] and more recently from the reaction of nitriles and chlorine [17] as shown in Figure 1.

Nitrosamines

Among various nitrosamines, *N*-nitrosodimethylamine (NDMA) is the most studied owing to its high toxicity,

Figure 1



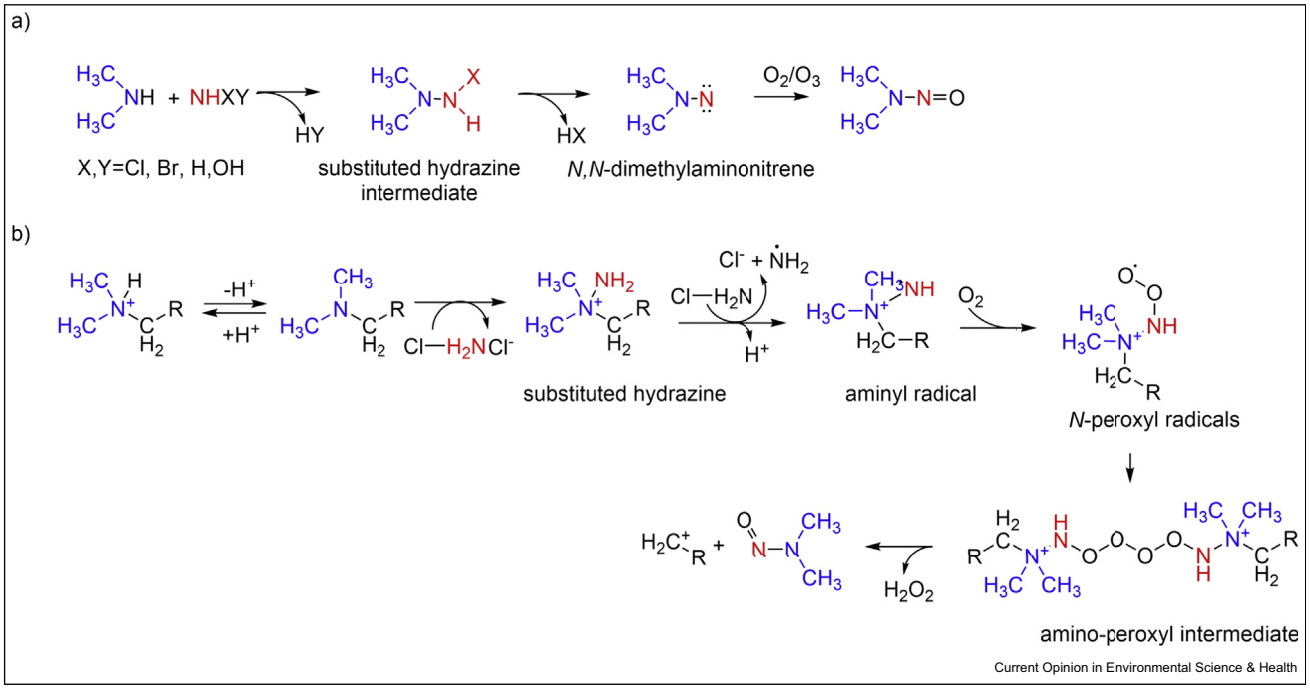
Formation and degradation pathways of *N*-chloramino acids and *N*-chloraldimines [11,12] and formation pathways of *N*-chloralkanolamines and *N*-chloramides [15–17].

common occurrence in disinfected waters, and strict regulations and guidelines. In a recent review on nitrosamines, many precursors were identified, with dimethylamine serving as the model precursor for most reaction mechanisms [18]. In a computational study, Liu and Zhong calculated thermodynamic free energies and enthalpies of formation for dimethylamine reactions via chloramination and ozonation as shown in Figure 2a [19]. Of the six species evaluated for their reactivity toward dimethylamine via chloramination, dichloramine and bromochloramine were found to be the most reactive. *N,N*-dimethylaminonitrene was identified as a key intermediate in NDMA formation via oxidation reactions by ozone and molecular oxygen. These results agree with findings of two other studies that identified dichloramine as the main oxidant which react with tertiary amines to predominantly form NDMA [20,21]. The results suggest that NDMA's formation is largely contingent on the presence of dichloramine as the primary oxidant, where monochloramine yields are less significant.

Spahr et al. [22] investigated the reaction between monochloramine and tertiary amines that lead to NDMA formation as shown in Figure 2b. Two model tertiary amines were studied owing to their high NDMA yields: ranitidine and 5-(dimethylaminomethyl)furfuryl alcohol. The authors proposed that the formation of NDMA occurs via transient intermediates including a substituted hydrazine and aminyl and amino-peroxyl radicals (Figure 2b). Molecular oxygen had a key role in the formation of amino-peroxyl radicals. Subsequently, the same authors investigated the isotope fractions of nitrogen, carbon, and hydrogen to infer NDMA formation mechanisms from the reaction of tertiary amines and monochloramine [23,24]**. The change in the isotopic ratios of two isotopically distinct monochloramine batches (NH_2Cl) and its organic precursors was analyzed using gas chromatography-isotope ratio mass spectrometry. The authors found that the nitrogen from NDMA originates from the tertiary amine moiety of the organic precursor, and the nitrogen from the nitroso group originates from monochloramine.

NDMA formation in water reuse treatment and water storage facilities were both investigated by Zeng and Mitch [25,26]. Zeng and Mitch [25] investigated the effect of biofilms on NDMA formation in water storage facilities. It was found that nitrifying samples resulted in elevated nitrite concentrations, low ammonia concentrations, and a decreased chloramine residual compared with samples that had not been nitrified. Breakpoint chlorination was found to produce lower NDMA and total nitrosamine concentrations, which can serve as a mitigation strategy in distribution systems. McCurry et al. [26] discovered that water quality conditions after reverse osmosis (low pH and low NH_4^+) helps promote the formation of dichloramine. Dichloramine can then react with organic precursors to re-form NDMA in water reuse applications. To limit this process, the authors

Figure 2



Proposed NDMA reaction mechanisms by Liu and Zong **(a)** and Spahr et al. **(b)** [18,19,22–24]. NDMA, *N*-nitrosodimethylamine.

suggested an immediate pH adjustment after reverse osmosis to help minimize NDMA formation.

Haloacetamides, haloacetonitriles, and halonitromethanes

Several studies have investigated the formation of N-DBPs from the reaction of disinfectants with organic precursors of anthropogenic [27–29] and natural [30–32] origins. Chlorination of antibiotics including chloramphenicol, thiamphenicol, and florfenicol produced high yields of dichloroacetamide compared with free and combined amino acids [27]. Chloramination of isolated aromatic fractions from DOM was also found to be important precursors to dichloroacetamide [30]. The study found that chloramine incorporation into DOM, which led to the production of N-DBPs, correlated with high specific ultraviolet absorbance values related to high aromaticity. Another interesting investigation examined the role of copper corrosion products (Cu_2O/Cu^{2+}/CuO) in the formation of brominated DBPs [31]. These products, prevalent in distribution systems, were found to catalyze the formation of brominated DBPs including haloacetamides and bromate in the presence of chlorine and bromide ions. A recent review article summarizes the impact of metal ions, metal oxides, and nanoparticles on the formation of DBPs [33].

Nitrogen-based intermediates and products

Dissolved organic nitrogen is an important precursor that leads to the formation of inorganic and organic amines. Recently, von Gunten's research group published two studies on (1) the formation of inorganic nitrogen compounds from ozonation and (2) the formation of inorganic and organic halamines and their subsequent reactions with organic compounds [34,35]. The first study examined the formation of nitrate and ammonium from the ozonation of DOM [34]. The authors found that nitrate formation was induced by an oxygen transfer to nitrogen forming hydroxylamine and oxime, while ammonium formation was induced by electron transfer reactions involving C-centered radicals and imine intermediates. In the second study, it was found that halamines quickly formed from the reaction of ammonia, methylamine, and dimethylamine with chlorine and bromine [35]. The halamines were found to be very reactive toward phenolic compounds, forming halogenated phenols via electrophilic aromatic substitution or quinones via electron transfer. However, halamines were outcompeted by faster chlorination and ozonation reactions and therefore may not be significant under normal water treatment process conditions.

DBPs derived from AOPs

Reactive halogen species

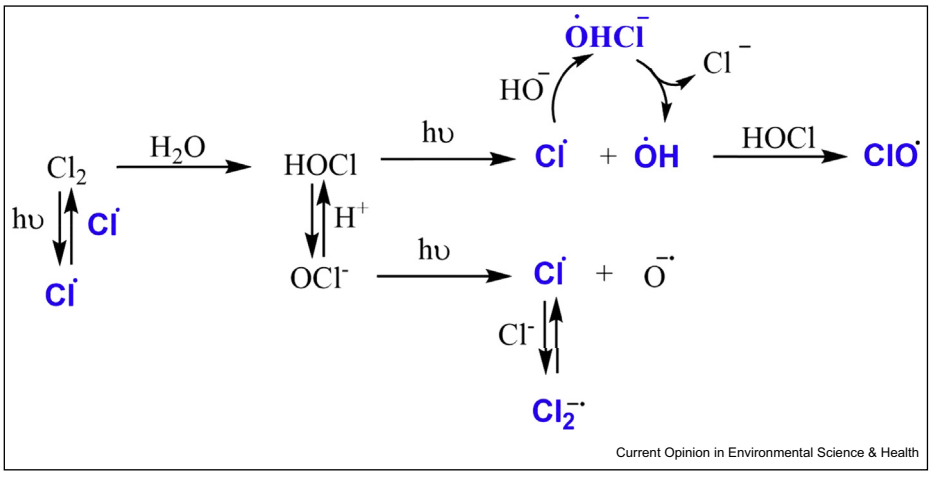
The formation of DBPs is largely determined by the reactive halogen species (RHS) that are added, produced, and transformed in natural and engineered processes. Yang and Pignatello [36] published a review on radical and nonradical RHS produced by sunlight-initiated reactions and by AOPs used for water treatment. The formation of RHS and subsequent reactions are discussed, including the role of RHS in the major pathways involved in the incorporation of halogens into organic matter and compounds. In a recent study, Hao et al. [37] studied the formation of organobromine and organoiodine compounds from photohalogenation of DOM that take place in natural systems. Mixed RHS (i.e. BrCl, $BrCl^{-\bullet}$, ICl, and/or $ICl^{-\bullet}$) were proposed as possible contributors to the increased formation of halogenated organic compounds observed in artificial seawater compared with freshwater. Organobromine compounds were formed mainly via substitution and addition reactions, while organoiodine compounds were produced through electrophilic substitution of aromatic protons. While these reaction mechanisms are derived from natural systems, they provide important mechanistic insights that may also apply to engineered systems.

Combined UV/chlorine and UV/chloramine

In recent years, there has been growing interest in combined UV/chlorine and UV/chloramine disinfection processes for their potential to degrade persistent pollutants faster than UV, chlorination, or chloramination alone. However, their potential to produce halogenated byproducts is a serious concern. Several studies have characterized the byproducts (i.e. chloroform, chlorinated phenols, and N-DBPs) from combined UV/chlorine disinfection of natural [38] and anthropogenic compounds [39–43]. Combined UV/chlorine is a serious concern, as combined approaches were confirmed to produce higher levels of DBPs than individual treatments, which could result in higher overall water toxicity. To understand the potential effects of new water treatment technologies, more studies are needed that simultaneously determine byproduct formation and gauge the resulting overall water toxicity. Reactive chlorine species including $Cl^{\bullet}$ [38], $Cl_2^{\bullet-}$ [40], and $ClO^{\bullet}$ [40,43] were proposed as the main contributors for pollutant degradation. Generation of hydroxyl and chlorine radical species by UV/chlorine is shown in Figure 3.

Recent studies have investigated the chlorine-derived radical reactions that take place in combined UV/chlorine [44,45] and UV/chloramine [46] processes, which provide mechanistic insights into these reactions [44,45]. Using computational methods, Minakata et al. [44]** calculated free energies of reaction and compared them with 22 chlorine-derived inorganic radical reactions that were experimentally determined from combined UV/chlorine. The analysis found a large discrepancy among literature-reported reaction rates. The study proposes that major reaction mechanisms

Figure 3



Generation of hydroxyl and chlorine radical species from combined UV/chlorine [36,44,45].

between $Cl^{\bullet}$ and organic molecules are via hydrogen abstraction and chlorine adduct formation. In another study, Guo et al. [45]* analyzed 34 pharmaceuticals and personal care products (PPCPs) by grouping them according to their reactivity with hydroxyl radicals ($HO^{\bullet}$) and reactive chlorine species ($Cl^{\bullet}$,$Cl_2^{\bullet-}$ and $ClO^{\bullet}$), which are generated in UV/chlorine processes. The authors found that reactive chlorine species showed significant reactivity toward olefins and benzene derivatives, such as phenols, anilines, and alkyl alkoxybenzenes. However, these reactions were affected by the water matrix. Specifically, DOM decreased the degradation of PPCPs attributable to $ClO^{\bullet}$, while alkalinity inhibited PPCP degradation via reactions that involved $HO^{\bullet}$ and $Cl^{\bullet}$. Chuang et al. [47] quantified the quantum yields for radical generation by UV photolysis of HOCl, OCl^{-}, and NH_2Cl and found to be lower than those reported in literature. The authors highlight the importance of incorporating $ClO^{\bullet}$ in kinetic models and other intermediates (i.e. ClO_2^{-}) to accurately model oxidant decay. Furthermore, Gleason et al. [46] investigated reactions relevant to UV/chloramination including OH radicals with monochloramine, dichloramine, and trichloramine. The authors proposed that $HO^{\bullet}$ reacts with monochloramines and dichloramines by H-abstraction to form $^{\bullet}NCl_2$ and $^{\bullet}NHCl$, while $HO^{\bullet}$ reacts with trichloramine by Cl abstraction to form $^{\bullet}NCl_2$. Overall, understanding intermediates and their reactivity with organic compounds is important in the evaluation of new water treatment technologies, especially the identification of potential undesirable side-effects from their application.

Total organic halogen

Total organic halogen (TOX) is a critical measurement that captures all the organic halogenated material including persistent organic pollutants and DBPs. TOX can be separated and quantified by the halogen type, that is, total organic chlorine (TOCl), total organic bromine (TOBr), and total organic iodine (TOI). TOCl, TOBr, and TOI are extremely valuable water quality parameters because brominated and iodinated organic compounds are generally much more toxic than chlorinated organic compounds. By capturing the entire halogenated organic fraction, both known and unknown compounds, the quality of surface and treated waters can be evaluated in a holistic way. Two studies investigated the mechanistic aspects of TOCl, TOBr, and TOI formation. Langsa et al. [48] investigated bromine incorporation into DOM. In this study, hypobromous acid (HOBr) was found to react via electrophilic substitution (<40%), forming TOBr, while the remaining HOBr reacted with DOM via electron transfer (>60%) with a reduction of HOBr to bromide ion (Br^{-}). Free chlorine (HOCl) can then reoxidize the released Br^{-} to HOBr and subsequently be incorporated as TOBr (>87%). A new pathway was proposed where chlorine-substituted DOM may be substituted by HOBr to form mixed Cl-Br-DOM moieties. In the first study of its kind, Zhu and Zhang [49] developed a comprehensive kinetic model that can predict the formation of TOCl, TOBr, and TOI by chlorination and chloramination [50]. This model suggests that I-DBPs formed by chlorination are converted to brominated and chlorinated DBPs by substitution reactions with HOBr and HOCl. The authors also propose that I-DBPs are formed by chloramination through a chloroiodoamine intermediate.

New methods and key intermediates in DBP formation

DBP formation via chemical reactions between organic precursors and disinfectants involves many intermediates, which are not always easy to identify, let alone measure and study. Creative analytical [13,14,23,24,51] and computational methods [19,44] have been developed and applied in recent years to elucidate important DBP formation mechanisms. For example, commonly used quenchers, which do not either fully quench the oxidants (i.e. ammonium chloride) or degrade DBPs (i.e. sodium thiosulfate, ascorbic acid, and sodium sulfite), may result in analytical artifacts [52]. Lau et al. proposed 1,3,5-trimethoxybenzene (TMB) as a new quencher for HOCl and HOBr. TMB was successfully used as a halogen quencher in kinetic studies involving chlorination and bromination of 2,4-dichlorphenol, anisol, and dimethenamid-P. Additionally, TMB did not degrade highly unstable DBPs including chloropicrin, bromoacetonitriles, and trihaloaldehydes [51]*.

Most chlorination and chloramination mechanistic studies emphasize the main oxidant species HOCl, NH_2Cl, and $NHCl_2$. However, free chlorine and chloramines may interact with water and other constituents to form a diverse set of oxidant species. Other species that are less studied but may play an important role in the formation of DBPs include halamines [18,35], chlorine (Cl_2), and dichlorine monoxide (Cl_2O) [53,54]. Lau et al. [53] investigated the role of Cl_2O and Cl_2 on phenol chlorination reactions. The authors found that chloride ion (Cl^-) concentration influences the formation of Cl_2, which contributes up to 80% of the overall phenol chlorination rate. Trace amounts of Cl^- can act as a catalyst in chlorination reactions. In another study, Broadwater et al. investigated the reactivity of various bromine and chlorine species (BrCl, BrOCl, Br_2, Br_2O, Cl_2, and Cl_2O) with salicylic acid, a human metabolite of aspirin detected in wastewater and surface waters. All the halogenating species studied were found to be more reactive compared with HOCl and HOBr [54]. Chloride ions were also found to promote higher chlorination and bromination rates through increased Cl_2 and BrCl formation, respectively. Heeb et al. [55] reviewed key bromine intermediate species and DBP formation mechanisms relevant to bromide-containing waters. These studies highlight the importance of other halogenating species beyond the main chlorine and chloramine species in DBP formation mechanism investigations.

Conclusions

Recently, most studies on DBP formation mechanisms have focused on those with higher toxicities and elevated human health risks, as well as their subsequent reactions with organic compounds. This includes organic amines and *N*-halamines, haloacetamides, haloacetonitriles, NDMA, and radical chlorine species. Additionally, new analytical methods that can accurately identify and quantify unstable DBPs, kinetic models that can comprehensively predict TOX formation, and computational methods that allow a deeper understanding of DBP reactivity have been added to the DBP toolbox. Previously overlooked formation mechanisms (i.e. *N*-halamino acids and *N*-halamides), oxidative species (Cl_2O and NHBrCl), and key intermediates (NDMA intermediates) that influence DBP formation were recently reported. Also, reactions derived from newly proposed water treatment technologies, namely combined UV/chlorine, still need to be thoroughly investigated before implementation. Important reactions that are not well understood include the complex formation of reactive chlorine species and their subsequent reactions with organic compounds. Closing knowledge gaps in DBP formation mechanisms will help water professionals and scientists to develop strategies to minimize DBP formation, reduce overall water toxicity, and improve water safety.

Conflict of interest statement

Nothing declared.

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